Dietary protein to support active aging

VALORIZATION

The age-related loss of skeletal muscle mass and strength, termed *sarcopenia*, increases the risk of disease development, hospitalization, and loss of independence in our older population. It is expected that the population over 65 years of age will triple in the upcoming 40 years. Together, the prevalence of sarcopenia and expansion in our older population will overburden existing health care systems. In order to maintain good health in our older population and offset the associated increase in health care costs, we must develop and apply strategies targeted at counteracting the progression of sarcopenia.

Older individuals display a blunted muscle protein synthetic response to protein ingestion, termed *anabolic resistance*, which is a major factor contributing to the loss of skeletal muscle mass. It is therefore evident that effective strategies should be targeted at compensating for the presence of anabolic resistance in our older population. In the present dissertation, we provide further evidence in older men that a bout of resistance-type exercise potently increases muscle protein synthesis rates (**Chapters 4 and 7**) and that prolonged resistance-type exercise training substantially increases skeletal muscle mass and strength (**Chapter 8**). As such, it is clear that participation in a resistance-type exercise training program should form the basis for nearly all strategies aimed at preserving skeletal muscle mass and strength in the older population.

Protein ingestion following exercise further increases muscle protein synthesis rates during post-exercise recovery. The amount of protein ingested following exercise is arguably the key nutritional factor dictating the magnitude of the increase in post-exercise muscle protein synthesis rates. However, the amount of ingested protein required to stimulate near-maximal post-exercise muscle protein synthesis rates has not yet been fully defined for the older population. Within the present dissertation (**Chapter 2**), it was demonstrated that older individuals require the ingestion of meals containing 30-45 g of protein is required to stimulate a near-maximal muscle protein synthetic response during post-exercise recovery.

Considering that most people ingest 3 meals per day, the ingestion of meals containing 30-45 g protein would result in a daily protein intake of 90-135 $g \cdot d^{-1}$, or 1.2-1.8 $g \cdot kg^{-1} \cdot d^{-1}$ in a 75 kg older person. Recent dietary intake data has revealed that habitual protein intake is 1.0-1.2 $g \cdot kg^{-1} \cdot d^{-1}$ in healthy, older individuals and 0-8-0.9 $g \cdot kg^{-1} \cdot d^{-1}$ in frail, older individuals (4). It is therefore apparent that increasing protein intake in older individuals may be practically challenging. However, there are a number of possible solutions that have been described to increase protein intake in various older populations. Aside from simply ingesting more food, older individuals could increase protein intake by co-ingesting isolated protein sources (e.g., protein shakes) with the main meals. Alternatively, protein-enriched food products appear to be an effective strategy to increase protein intake in various older populations (1, 2). Ingestion of isolated protein shakes and/or protein-enriched food products would be most effective if ingested with meals that do not typically contain more than 30 g protein, such as breakfast and lunch (4). Dietary intake data has also revealed that older individuals do not ingest protein in the evening (4). It has therefore been proposed that protein ingestion prior to sleep may represent an opportunity to increase dietary protein intake in the older

population. We report in the present thesis (**Chapter 4**) that pre-sleep protein ingestion is properly digested and absorbed and, when combined with physical activity, robustly increases overnight muscle protein synthesis rates. These data provide further support that pre-sleep protein ingestion may represent an effective nutritional strategy to compensate for anabolic resistance.

Aside from strategies aimed at increasing dietary protein intake, co-ingestion of certain single nutrients appears to augment muscle protein synthesis rates when smaller protein doses are ingested (5). In **Chapter 3** of the present thesis, we demonstrate that free leucine co-ingestion with 15 g protein stimulates greater muscle protein synthesis rates compared with ingestion of only 15 g protein during post-exercise recovery in the older population. As such, older individuals may also compensate for insufficient dietary protein intake by co-ingesting each meal with a small amount of free leucine. This may be of particular relevance in certain older populations that struggle to consume adequate amounts of protein intake. Development of products containing free leucine (e.g., dissolvable powders, beverages, desserts, pills, gum, gels) represents a practical approach for implementation of free leucine co-ingestion in the general population. Alternatively, future product development should explore the efficacy of fortifying food products with free leucine to augment the anabolic response to meal ingestion.

Older individuals are far more likely to be admitted to the hospital when compared to the younger population. Short-term hospital stays necessitate bed rest, which can dramatically accelerate the progression of age-related skeletal muscle mass and strength loss (3). While in bed, hospitalized patients spend most of the time lying in a supine body position. It is known that the digestibility of protein sources can modulate the post-prandial rise in circulating amino acid concentrations, which thereby impacts post-prandial muscle protein synthesis rates (6). We demonstrated in the present thesis (**Chapters 5 and 6**) that protein digestion and absorption is impacted by body position. In particular, we found that peak leucine concentration and plasma amino acid availability was greater when protein was ingested in an upright, seated position when compared with a supine, lying position. It is proposed that consuming food in an upright body position may promote a greater increase in post-prandial muscle protein synthesis rates. Current clinical nutrition protocols do not typically incorporate guidelines regarding the body position of patients during feeding. Based on early findings, however, future research should investigate the impact of body position on post prandial muscle protein synthesis rates in more clinically compromised populations. Knowledge on this topic could be used to innovate currently existing clinical nutrition guidelines to accelerate recovery and attenuate the age-related loss in skeletal muscle mass and strength in a variety of populations. Such innovation may be as simple as providing hospital patients with a communal dining space to encourage patients to sit (upright) while eating meals.

Even though the benefits of resistance-type exercise training and dietary protein intake on skeletal muscle mass and strength may be widely known, they are not yet considered by the

general public to be relevant for older individuals. With this in mind, we must first implement strategies to educate older people to recognize the importance of maintaining skeletal muscle mass and strength. Along with improving awareness, we also need to provide our older population with an environment to better facilitate participation in exercise training. This knowledge translation to the general public and facilitation of exercise participation will likely be most effective if carried out through large-scale collaboration. For example, scientists are required to generate data to demonstrate the health implications of skeletal muscle loss and better understand the efficacy of novel exercise and dietary interventions to counteract skeletal muscle loss. Medical and scientific societies are required to incorporate relevant scientific findings into current public guidelines for healthy lifestyle. Considering the proposed financial burden of age-related muscle loss on existing healthcare systems, implementation of national-level exercise programs would offset the projected increase in age-related health care costs. Therefore, governmental intervention is required to develop and introduce new policies and fund programs aimed at educating and implementing strategies to increase muscle mass and strength in the older population. Additional financial support may be attained by insurance companies as older individuals in good health would presumably continue contributing to insurance policies as opposed to drawing insurance claims. Funding should be targeted to support construction of new facilities that are readily available to the general public and possess the capacity to support the coming expansion in the older population. Current nutritional information, some of which has been described in the present thesis, and advice should be provided at fitness facilities to maximize the health benefits of exercise training. Provision of this information should occur though professional health practitioners, which include: kinesiologists and registered dietitians, as well as physicians, nurses, and personal care-givers.

Personal perspective

It is clear that we must develop a deeper understanding of skeletal muscle tissue deconditioning that occurs over the lifespan. With this knowledge, we can better design intervention strategies to counteract skeletal muscle mass loss and the associated negative health consequences. While we have developed an understanding of age-related skeletal muscle mass loss on a whole-body level, the impact of aging on the regulation of skeletal muscle protein reconditioning still remains unclear. As discussed in **Chapter 9**, the application of deuterated water (**Chapters 7 and 8**) improves isotopic label detection in peptides, allowing simultaneous assessment of *in vivo* synthesis rates of several individual skeletal muscle proteins. This technique has been termed *dynamic proteomics*. Individual skeletal muscle protein regulation determines whole-body metabolic and functional consequences. Therefore, application of the dynamic proteomics method in older individuals will allow for the determination of dysregulated individual protein translation that is associated with aging. Subsequent investigation into the impact of various exercise and

nutritional intervention strategies will provide us with a better understanding of how such strategies counteract the dysregulation and contribute to improvements in metabolic health and physical function. Further exploration will allow us to optimize intervention strategies so that we can more effectively counteract the progression of sarcopenia. Investigation into the impact of aging and short-term muscular disuse on individual protein synthesis rates will be the focus of my post-doctoral work.

References

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